



## REVIEW

# Dysplasia, malformation, or deformity? - explanation of the basis of hip development disorders and suggestions for future diagnostics and treatment [version 1; peer review: 1 not approved]

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**V1** First published: 13 Oct 2020, 9:1231  
<https://doi.org/10.12688/f1000research.25598.1>  
Latest published: 26 Jan 2021, 9:1231  
<https://doi.org/10.12688/f1000research.25598.2>

## Abstract

This publication focuses on processes which disrupt proper development of the hip. Four pathomechanisms underlying human developmental defects are described in literature, i.e. dysplasia, malformation, disruption, and deformity. In the case of hip development, arguably the greatest challenge involves confusion between dysplasia and deformity, which often leads to misdiagnosis, incorrect nomenclature, and incorrectly chosen treatment. The paper presents a description of hip joint development disorders in the context of their pathomechanisms. An attempt was made to answer the question whether these disorders are rooted in a primary disorder of tissue growth, resulting in its incorrect anatomy, or are the result of anatomical deformation with secondary modifications in tissue structures of a degenerative or adaptive nature, based on Deplesch-Heuter-Volkman growth and remodeling laws. In addition, emphasis is placed on attention to the presence of the so-called clinically and diagnostically mute cases. The need to augment diagnostic procedures with genetic tests in order to increase the sensitivity of screening has also been suggested. Based on the arguments presented in the paper, a new division of developmental hip disorders has been proposed.

## Keywords

dysplasia, malformation, deformity, hip development disorder

## Open Peer Review

### Reviewer Status

Invited Reviewers

1

#### version 2

(revision)  
26 Jan 2021

#### version 1

13 Oct 2020

  
report

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**Author roles:** **Dygut J:** Conceptualization, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; **Piwowar M:** Investigation, Methodology, Resources, Writing – Original Draft Preparation, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**Grant information:** The author(s) declared that no grants were involved in supporting this work.

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**How to cite this article:** Dygut J and Piwowar M. **Dysplasia, malformation, or deformity? - explanation of the basis of hip development disorders and suggestions for future diagnostics and treatment [version 1; peer review: 1 not approved]** F1000Research 2020, 9:1231 <https://doi.org/10.12688/f1000research.25598.1>

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## Introduction

Many studies of hip development disorders have been performed<sup>1</sup>, leading to a number of proposed diagnostic and treatment options<sup>2</sup>. Despite the impressive collection of studies documented in scientific publications, the etiology of developmental disorders of the hip joint still cannot be formulated with clarity<sup>1,3–5</sup>. Even so, the etiology of these diseases is known to be multifactorial, combining genetic factors (with varying intensity and expression periods) and environmental factors affecting the fetal and postnatal periods<sup>6,7</sup>. Normal hip growth and development depend on a genetically determined balance between the growth of the acetabular and tri-radiate cartilages and a properly located and centered femoral head<sup>6,8,9</sup>.

Experimental studies have revealed that the development of the acetabulum depends on a coded geometric pattern<sup>10,11</sup>. The concave shape of the acetabulum results from the presence of a round femoral head inside. In addition, many other factors affect the acetabular depth, including growth within the acetabular cartilage, growth through apposition under the perichondrium layer, and growth of adjacent bones (iliac, sciatic and pubic)<sup>8,9</sup>.

The incidence of developmental hip growth disorders varies by population. It is close to 0% among newborns in China and Africa, but rises to 1% in Caucasian newborns, with the incidence of hip dislocations at approximately 0.1%<sup>12</sup>. Notably, these differences may result from environmental factors, such as the manner of childcare, rather than genetic issues. A positive family history of hip development disorders is found in 12–33% of patients and is more often observed in female children (80% of cases)<sup>12</sup>.

As described in literature, three independent but equivalent pathomechanisms underlying hip joint development disorders, i.e. malformation, dysplasia, and deformity, can be identified<sup>4</sup>. The fourth pathomechanism of developmental disorders – disruption – has been excluded from further considerations because its relevance to developmental hip disorders remains unproven. With the exception of deformity, which falls within the group of so-called “packaging problems”, the three remaining pathomechanisms are collectively referred to as “production problems”<sup>12</sup>.

Many recent scientific reports do not take into account the differences between the above-mentioned pathomechanisms. An equality sign is placed between them, treating them as synonyms usually grouped under one name, i.e. developmental dysplasia of the hip (DDH)<sup>13–15</sup>. Some publications use the following terms interchangeably: congenital hip dysplasia<sup>3</sup>, congenital hip dislocation<sup>16</sup>, developmental deformity of the hip<sup>17</sup>. Others contain statements such as “... malformation of anatomical structures occurs in dysplasia, which at the time of embryonic development were still normal ...” or “...developmental hip dysplasia is more deformity than malformation ...”<sup>12</sup>. According to the International Classification of Diseases

and Health Problems (Q65 to Q79), the term “congenital hip dislocation” remains valid<sup>18</sup>.

To precisely explain the need to distinguish and organize these issues, we present and explain the following definitions, based on which a new division of hip developmental disorders is proposed.

**A congenital defect** is a disorder present since birth. It is a general term, broadly describing the structural, behavioral, functional and metabolic damage that occurred in prenatal life, and which is diagnosed after birth or later in life<sup>19</sup>.

**Malformation** (Latin: *malformatio*) is a term frequently used by English-speaking authors to refer to developmental disorders in general. More specifically, however, malformation represents just one of the four pathomechanisms of developmental disorders<sup>4</sup>. Malformation concerns developmental disorders, but only during the embryonic period. Referring to developmental changes which occur after this period as “malformation” is incorrect.

Malformation of the mesenchymal primordium of the hip joint is a type of birth defect caused by a primary disorder of hip development during the embryonic period, during differentiation or organogenesis. The primary disorder affects cell proliferation, differentiation, migration, apoptosis or cell inter-communication processes. Primary impairment of cell function inhibits, delays or directs tissue development in the wrong direction, causing improper formation of anatomical structures of the hip<sup>4</sup>. Malformation underlies the development of congenital teratogenic hip dislocation.

**Dysplasia of the hip** is a type of disorder in which abnormally developing tissue (often excessively flaccid) results in faulty hip anatomy and evolves over time. Anatomical structures of the hip, normal during embryonic development, gradually become abnormal for various reasons<sup>10,20</sup>. Dysplasia may be environmentally or genetically conditioned. Dysplastic changes, along with malformation and disruption, may be collectively referred to as “production problems”. Hip dysplasia can occur both in the prenatal (early dysplasia) and postnatal (late dysplasia) period<sup>21</sup>. These disorders do not tend to self-heal<sup>12</sup>.

**Deformity of the hip joint** is an example of a developmental disorder in which properly developed structures are deformed during growth, as a result of mechanical factors. This can occur both in the pre- and postnatal periods. If the mechanical factor is active in the prenatal period, then we may refer to it as a “packaging problem”, associated with intrauterine fetal modeling. Disorders of this type are unlikely to cause growth disorders – rather, they tend to disappear with age and self-heal<sup>12</sup>.

**A developmental disorder** is disorganization in the anatomical structure of the osteoarticular system that appears after some time, is absent or invisible at birth and has a tendency to either self-heal or worsen over time. In English literature, the

term “structural defect” is often used in the context of developmental disorders to emphasize the anatomical nature of the defect.

When referring to dysplasia and deformity, it is reasonable to introduce an additional term – “developmental disorder” – because we are talking about anomalies with a tendency to self-heal or become more severe over time<sup>4</sup>. Developmental dysplasia or developmental deformity of the hip, depending on the time of occurrence, can be early (primary – invisible and present at birth) or late (secondary – absent, and appearing after some time)<sup>12</sup>.

As disruption has not been described in the context of developmental hip joint disorders, and malformation is relatively easily diagnosed as a component of congenital anomalies, the main focus is on the distinction between dysplasia and deformity.

The aforementioned distinction is extremely important because it projects the course of treatment and prognosis of hip joint development disorders. It influences the choice of various conservative or surgical treatment strategies aimed at maintaining or restoring the normal growth potential of anatomical structures<sup>12</sup>. Misdiagnosis can lead to incorrect therapeutic management and, consequently, to deepening disability, thus significantly increasing the cost of treatment<sup>22,23</sup>.

The following is a discussion of the pathogenesis of developmental hip disorders with a focus on dysplasia and deformities.

## Discussion

### Malformation as a disorder of the hip joint formation process

The pathomechanism of malformation cannot be the root cause of developmental hip disorder leading to dysplasia because it is only in the seventh week of life within the mesenchyme that the hip joint develops a fissure secreting the future femoral head and the acetabulum. Therefore, the first period when hip dislocation, and thus developmental hip dysplasia, may occur is the eleventh week of fetal life – the time when the hip joint is fully formed<sup>6</sup>. In the case of malformation, the most frequent causative factor is congenital anomalies syndrome, which generally does not pose major diagnostic difficulties. The effects of such congenital changes are present and visible immediately after childbirth<sup>24</sup>.

### Dysplasia and deformity as developmental disorders of the hip joint

In the literature, dysplasia is considered in two aspects: dysplasia as a precancerous lesion (applies only to epithelial tissue, which is outside of the scope of this discussion), and dysplasia as a developmental disorder, involving incorrect organization or function of cells in a specific tissue (described as “production problems”), which is under consideration<sup>12</sup>. Dysplasia, which is a developmental disorder of the hip, can be grouped under the so-called **osteoarticular dysplasia**

**epiphyseal type**<sup>20,25</sup>. It is characterized by abnormal growth potential of tissue structures underlying anatomical and functional changes in the growing hip<sup>8,9</sup>. In such cases, using the term **dysplasia** is fully justified.

Risk factors for developmental dysplasia can include environmental or genetic conditions on both the mother and child side. Many scientific reports contain information on the impact of elevated level of biochemical factors on the occurrence of developmental dysplasia, e.g. female hormones (e.g. relaxin, estrogens) and biochemical markers of nutritional status (e.g. calcium, vitamins C and D)<sup>1</sup>. Regarding the relationship between the concentration of the hormone relaxin derived from the mother in the blood of the fetus and instability of hip joints, it was established that facts contradict the earlier assumption that hip instability coincides with increased relaxin concentrations in newborns. Instead, results indicate that hip instability frequently accompanies decreasing relaxin levels. The authors therefore assumed poorer mobilization of the pelvis and the birth canal during pregnancy as a result of the lower concentration of relaxin, which may result in greater pressure on the fetus in the perinatal phase<sup>26</sup>. Abnormalities caused by the disturbed balance of biochemical factors on the part of the mother can be expressed in the immaturity of the tissues of the child’s hip joint and the delay of their development in the prenatal period<sup>26–28</sup>. Such changes may be temporary and transient. With the right positioning of the hips, proper care of the newborn and then the baby, in most cases, the correct architecture of the anatomical elements of the hip can be restored<sup>7</sup>.

Other studies report genetic disorders of the fetus underlying dysplastic changes in the hip joints. It has been confirmed that relaxation of ligaments and joint capsules, as well as irregularities in collagen metabolism, are associated with developmental dysplasia.

It has also been shown that some types of HLA A, B, and D, as well as mutations in specific genes or regulatory sequences, including genetic changes on chromosome 17 (17q21), predispose the child to developmental hip disorders of a dysplastic nature<sup>5,29,30</sup>. This group likely covers cases of developmental disorders characterized by prevalence of residual, recurrent and late forms that are resistant to treatment.

In situations (as assumed by the Delpesch law) where a correctly growing hip joint is affected by an external mechanical force, whether intracorporeal (e.g. extra-articular contracture) or extracorporeal (e.g. incorrect position of the lower limb), leading to deformation of its anatomical structure, we are dealing with deformity<sup>12</sup>. Prolonged action of such factors, combined with ongoing growth, may result in ultimate subluxation or even full dislocation. In such cases, the term “deformity” is fully justified.

In deformity, change in the shape of the growing hip joint due to external extra-articular forces is not accompanied by disruption of the structure and tissue function in the initial phase,

as is the case with dysplasia. Uneven distribution of forces acting on the roof of the growing acetabulum by the moving head leads to inhibition of growth of cartilage and bone tissue, their sclerosis and ultimately steep positioning of the acetabulum roof<sup>10</sup>. Atrophy of the acetabulum roof is accompanied by excessive bone growth within its fossa, i.e. in the unloaded zone. As a result of the loss of modeling and sliding out of the femoral head during acetabulum growth, the acetabulum bottom becomes bold, the acetabulum roof flattens and the acetabulum becomes shallow.

These processes of growth and remodeling of cartilage and bone tissue are of a secondary character and comply with Wolff-Delpesch laws, later developed by Hueter-Volkman, Pauwels, and Arndt-Schmidt<sup>12</sup>.

The Hueter-Volkman law also explains the presence of the most frequently observed pathological change in early post-natal hip dislocation, which is neolimbus (Ortolani positive symptom)<sup>6,12</sup>. The lack of physiological interaction (mutual pressure) between the head and the posterior edge of the acetabulum leads to excessive hypertrophy of the hyaline cartilage (neolimbus) in the upper, posterior and lower periphery of the acetabulum with the labrum curved out (pulled by a joint capsule in the dislocated hip)<sup>12</sup>.

Deformity caused by mechanical factors, which is usually the result of intrauterine modeling, especially in the last trimester of pregnancy (hence the term “packaging problems”) usually does not cause disturbances in the growth potential of joint tissues, as observed in dysplasia or malformation. Instead, it exhibits a tendency to self-heal and rarely leads to relapse<sup>12</sup>.

This group includes cases of fetuses with abnormal breech position and ultra-position of limbs which self-heal or recover in the postnatal period, assisted by short-term conservative therapy<sup>7</sup>. Treatment involving restoration of the compact joint with concentric maintenance of the head in the acetabulum ensures optimal development conditions. If reposition is effectively maintained, the acetabulum, femoral head and femoral neck in intervention undergo remodeling as a result of their normal growth potential. Restoration of the correct and stable joint connection between the femoral head and the acetabulum can lead to remodeling of the deformity and normalization of the morphology of the hip (due to developmental plasticity)<sup>12</sup>. The potential and growth time of the hip joint are closely related and depend on genetic and environmental factors<sup>12</sup>. These include genetic variations, e.g. of the SNP type, modulating the activity of proteins important from the point of view of tissue function, along with factors such as nutrition, general health, hormone concentration, mechanical forces and physiological age<sup>30</sup>. Therefore, during diagnostics and treatment, dysplastic and deformative cases should be considered together.

Time can be an ally or an enemy, depending on whether growth potential remains normal. If it does, as in the case

of deformity, then growth may promote development of correct anatomical structures (after correction and concentric arrangement of the elements of the hip joint). In the absence of normal growth potential, as with dysplasia, deformity of anatomical structures may deepen<sup>12</sup> as growth progresses, even if a concentric position of the hip is achieved (recurrent, residual dysplasia resistant to treatment).

### Clinically and diagnostically mute hip developmental disorders

It is nearly impossible to distinguish between dysplasia and hip joint deformity on the basis of physical examination and imaging, e.g. ultrasound, X-ray and MRI. The procedures used in many countries, which call for imaging when Ortolani, Barlow and limited abduction tests are positive, may not be sufficient<sup>12,15</sup>. Because of the difficulty in correctly distinguishing between these two pathomechanisms, misdiagnosis often follows, and terminology is incorrectly applied. In the diagnosis and treatment of developmental hip joint disorders, there is a notable lack of uniform diagnostic and therapeutic standards in various countries around the world. This applies to the frequency of examinations and their complementarity<sup>15,31–34</sup>. There is also the danger of not detecting so-called clinically mute developmental disorders<sup>6,35</sup>. These are cases in which physical examination does not provide information about pathological changes at the joint level, which, however, become evident under imaging<sup>15</sup>. Literature describes cases of otherwise healthy children with normal physical examinations and radiographs of the hip in the first 3 months of life, who later developed hip dislocations<sup>21</sup>.

The opposite situation – involving diagnostically mute developmental disorders – may also occur. This condition occurs when physical examination clearly indicates a developmental disorder of the hip joint, and even its total displacement, while additional imaging tests do not confirm such abnormalities<sup>21</sup>. The joint can be anatomically normal but functionally abnormal, e.g. due to limitation of hip abduction. Passivity towards asymmetrical movement of the hip abduction can lead to a developmental hip disorder which often results in dislocation<sup>15</sup>. In this context, it should be noted that in cases of developmental hip disorder dysplasia and deformity, physical examination remains the priority, but it must be supplemented with imaging tests. Complementarity of physical examinations and imaging tests may reduce the number of undetected diagnostically and clinically silent cases.

### Early detection of cases of late dysplasia

In many cases of dysplasia in the first weeks of the child's life, the doctor will not observe pathological anatomical changes of the hip and will not detect tissue changes despite the fact that they are present. These changes may lead to joint incongruity, deepening during hip development, as observed in late forms of dysplasia.

In the case of late dysplasia, diagnoses are most often made in a situation when there are degenerative changes in the hip joint presenting with pain in the 3rd or 4th decade of life<sup>6</sup>.



Treatment implemented at this stage is symptomatic and clearly less effective than it might have been had the problem been noticed earlier. In order to avoid such situations, the possibility of implementing additional diagnostic tests should be considered. Given the development of high-throughput methods and the corresponding decrease in their cost, it is worth considering the implementation of a genetic testing procedure for detecting genetic variations responsible for pathological phenotypes. Knowledge about the genotype of patients with dysplastic changes would facilitate therapeutic planning in early cases of dysplasia, particularly with regard to abnormalities which are not phenotypically revealed until a later period in the patient's life<sup>15</sup>. Such variations may explain the presence of short- and long-term tissue function disturbances, which lead to anatomical disorders of acetabulum development along with functional disorders of extra-articular tissues (contracture, excessive flaccidity)<sup>6,36,37</sup>.

Several papers have been published on the topic of the genetic background of hip dysplasia; however, these studies always focus on changes occurring in specific genes. A study of the full range of genomic sequences with all potential variations (NGS sequencing studies) would allow us to describe the entire spectrum of variations comprising of the observed dysplastic changes<sup>29,30</sup>. Identification of e.g. single nucleotide changes (correlated with pathological phenotypes and affecting regulatory sequences which modulate protein functions) could significantly increase the level of diagnostic accuracy<sup>38,39</sup>.

Considering the above facts, it should be noted that nowadays there may still be clinically and diagnostically mute cases in neonatal hip tests, since genetic diagnostics are not yet routine. Integration of genetic testing with medical procedures would enable objective assessment of the situation at an early stage in both early and late dysplasia.

Detection of differences at the level of genomic DNA, characteristic of the group of patients with dysplasia, would allow classification of this disorder with varying degrees of aggressiveness based on the obtained genetic profiles. In the future, this could serve as a tool for planning personalized therapy and become part of international standards<sup>15,31–34</sup>. Incorrect diagnosis resulting from incomplete patient data is the main cause of disability in childhood and adulthood, and treating such disability imposes a serious burden on state budgets<sup>40</sup>. With modern diagnostic tools the consequences of overlooking the defects could be largely avoided. In addition, this would sensitize the attending physicians to the possibility of late presentation of the abnormality, its resistance to treatment and eventual recurrence. Vigilance in the treatment process would facilitate thoughtful planning of the course of therapeutic management and thus improve the quality of life of patients in the future<sup>41</sup>.

### Classification of developmental hip disorders

Based on the above considerations, a classification of developmental hip disorders was proposed depending on the etiology of the defect.

## I. Developmental disorders of the hip joint associated with “production problems”

In these abnormalities, the tissues forming the hip joint are primarily defective (dysplastic). Primary disturbed tissue development results in secondary disturbed hip joint anatomy.

### 1) Teratogenic congenital hip dislocation

This is an example of a “tissue production” disorder which involves malformation at the embryonic stage, i.e. before the end of hip joint differentiation. It can be caused by genetic and/or biochemical and/or biophysical factors in the embryonic period.

### 2) Developmental dysplasia of the hip (DDH)

Another “tissue production” disorder involving dysplasia, which may begin to manifest in the prenatal (fetal) period, i.e. from the time of hip joint formation (at 11–12 weeks of age) throughout the postnatal period. It may be caused by genetic and/or environmental factors.

Depending on the time of onset, DDH can be divided into:

#### A) Early (primary) developmental dysplasia of the hip

This disorder refers to the fetal phase of the prenatal period including the postnatal period up until the end of the 3rd month of life.

#### B) Late (secondary) developmental hip dysplasia

This disorder refers to the postnatal period – after 3 months of age.

## II. Developmental disorders of the hip associated with so-called “packaging problems”

In these disorders, properly formed tissues of the anatomical structures of the hip joint are deformed due to prolonged presence of mechanical factors. An untreated deformity may, in the long term, cause secondary hip tissue changes in accordance with the remodeling and adaptation laws of Delpesch-Heuter-Volkman – this mainly concerns bone tissue (atrophy and sclerosis in the overloaded zone, hypertrophy and low-density bone structure in the unloaded zone)<sup>42</sup>.

### 1) Early (primary) developmental hip deformity

This disorder occurs in the prenatal (fetal) period and the postnatal period until the end of the 3rd month of life. Depending on the time of exposure to the deforming mechanical factor, we can distinguish a number of different risk factors. In the fetal period, these include: ultra position of the fetal lower limbs; breech position of the fetus; left hip joint – pressure on the sacrum prior to and during head delivery; oligohydramnios – intrauterine narrowness; primigravida.

Risk factors present in the postnatal period (up until the end of the 3rd month of life) include incorrect diapering and extra-articular contractures.

### 2) Late (secondary) developmental deformity of the hip

This disorder occurs in the postnatal period, after the 3rd month of life. Risk factors include improper care, neurogenic

disorders (e.g. disorders of muscular balance in cerebral palsy, myelomeningocele, perinatal neuromuscular dystonia), inflammatory conditions (e.g. viral or bacterial hip inflammation), extra-articular contractures within e.g. adductor muscles of the hip caused by: idiopathic muscle fibrosis, ionizing radiation fibrosis, postinflammatory fibrosis (viral muscle damage, bacterial descent processes after abscesses) and fibrosing postpartum hematomas.

### III. Developmental disorders of the hip associated with the so-called “packaging problems” and “production problems” (mixed)

In these disorders we deal with situations in which the deformity has a secondary effect on tissue quality, or deformity changes are superimposed upon dysplastic changes.

#### 1. Dysplastic disorder with secondary deformity changes

After birth, the dysplastic hip joint with a disturbed congruence is affected by an additional iatrogenic mechanical external force, e.g. associated with incorrect diapers.

#### 2. Deformity or dysplastic disorder with secondary degenerative tissue changes

Prolonged maintenance of untreated deformity or dysplasia and the resulting lack of joint congruence may result in secondary degenerative changes. These changes are a direct consequence of improper nutrition of joint and extra-articular tissues caused by pathological intra- and extra-articular forces.

### Conclusions

Dysplasia, malformation, and deformity are three of the four basic pathomechanisms leading to developmental hip disorders which are often not disambiguated at the clinical level and are therefore incorrectly named. Because malformation is relatively readable for the clinician, it is the least difficult to recognize. However, it is far more difficult to distinguish between dysplasia and deformity, because existing standards do not provide explicit methods along with a full range of diagnostic options. Nevertheless, this distinction is crucial and not merely a theoretical problem – it may influence medical practice, affecting patients' quality of life and reducing treatment costs.

To achieve this goal, it is necessary to perform a full diagnostic process (physical examinations, imaging tests, genetic tests) in the immediate postnatal period to determine whether we're dealing with:

- an anatomically normal hip joint with a normal growth potential
- teratogenic congenital dislocation of the hip with disturbed tissue growth potential in the malformation process (embryonic period)
- a dysplastic hip joint with disturbed growth potential in the prenatal period (fetal period) (cases of early dysplasia)
- an initially anatomically normal hip joint, but with a changed genotype that interferes with the potential for tissue growth in the postnatal period (cases of late dysplasia)
- a deformed hip joint with normal growth potential occurring in the pre- and postnatal periods (cases of early and late developmental deformities)
- a dysplastic hip joint with external deforming mechanical forces affecting it during the fetal or postnatal period
- a deformed or dysplastic hip joint which is affected by internal or external mechanical forces (joint dyscongruence) resulting in secondary degenerative tissue changes.

In addition to routine procedures, specialists will likely have to rely on additional genetic testing to account for the possibility of recurrent residual dysplasia refractory to treatment despite a properly managed therapeutic process. In addition, such tests may help quickly explain the specific type of dysplasia and late deformities, preventing premature termination of diagnosis and treatment and thereby improving the quality of life of patients. The presented procedure would reduce the percentage of undetected diagnostically mute dysplasia and deformity.

### Data availability

#### Underlying data

No data are associated with this article.

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# Open Peer Review

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Version 1

Reviewer Report 17 November 2020

<https://doi.org/10.5256/f1000research.28251.r72952>

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**Grzegorz Szczęsny**

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In the paper, the Authors discuss a quite controversial idea that developmental dysplasia of the hip is not a pure dysplasia, but partly belongs to a group of malformations, partly to deformities and partly to developmental disorders. Thus, they proposed their own classification of the DDH basing their idea.

Unfortunately, according to DDH, its classification of malformations, deformities or developmental disorders is very controversial, as DDH in fact does not fulfill the definitions of those conditions.

According to definitions given by several widely accepted sources, including <https://medical-dictionary.thefreedictionary.com/malformation>, <https://onlinelibrary.wiley.com/doi/pdf/10.1002/ajmg.a.36249> and Wikipedia, malformation is associated with a disorder of tissue development that often occurs in the first trimester. Deformation is equal to malformation (<https://medical-dictionary.thefreedictionary.com/malformation>).

Authors assumed that pathological changes that are observed in the hip joint affected by something that is nowadays called DDH could originate from malformation, deformity and developmental disorders. In the paragraph: "... *Many recent scientific reports do not take into account the differences between the above-mentioned pathomechanism. An equality sign is placed between them, treating them as synonyms usually grouped under one name, i.e. developmental dysplasia of the hip (DDH)*<sup>13-15</sup>. Some publications use the following terms interchangeably: congenital hip dysplasia<sup>3</sup>, congenital hip dislocation<sup>16</sup>, developmental deformity of the hip<sup>17</sup>. Others contain statements such as "... malformation of anatomical structures occurs in dysplasia, which at the time of embryonic development were still normal ..." or "...developmental hip dysplasia is more deformity than malformation ..."<sup>12</sup>. According to the International Classification of Diseases and Health Problems (Q65 to Q79), the term "congenital hip dislocation" remains valid<sup>18</sup>..." they use several footnotes that do

not confirm their theses. Moreover, literature positions 13, 14 and 15 do not discuss malformation, deformation, deformity nor developmental disorders et al. In the position nr 14, the words deformity and developmental disorder were used one time only each and in a totally different meaning than that presented by Authors of the analyzed publication.

The statement: "...Malformation of the mesenchymal primordium of the hip joint is a type of birth defect caused by a primary disorder of hip development during the embryonic period, during differentiation or organogenesis..." do not correspond to its definition, since malformation is associated with a disorder of **tissue** development. Disorders at the organ level are called dysplasia ([https://en.wikipedia.org/wiki/Birth\\_defect](https://en.wikipedia.org/wiki/Birth_defect)).

#### **Other inaccuracies:**

*"...The pathomechanism of malformation cannot be the root cause of developmental hip disorder leading to dysplasia because it is only in the seventh week of life within the mesenchyme that the hip joint develops a fissure secreting the future femoral head and the acetabulum. Therefore, the first period when hip dislocation, and thus developmental hip dysplasia, may occur is the eleventh week of fetal life – the time when the hip joint is fully formed<sup>6</sup>. In the case of malformation, the most frequent causative factor is congenital anomalies syndrome, which generally does not pose major diagnostic difficulties. The effects of such congenital changes are present and visible immediately after childbirth<sup>24</sup> ...".* Methinks that it is not especially the fissure of the hip joint that secretes femoral head and acetabulum. Both structures are rather formed in consequence of endochondral ossification of cartilaginous structures of the three pelvic bones at the ypsilon cartilage and femoral head. *"...dysplasia as a precancerous lesion..."* could hardly be proven. Authors should focus on the subject of their paper - that is on hip dysplasia.

The paragraph *"...Early detection of cases of late dysplasia. In many cases of dysplasia in the first weeks of life, the doctor will not be able to observe clinically pathological signs and thus will not be able to "detect ... dysplasia" despite the fact that they are present. These changes may lead to joint incongruity, deepening during hip development, as observed in late forms of dysplasia.*

*In the case of late dysplasia, diagnoses are most often made in a situation when there are degenerative changes in the hip joint presenting with pain in the 3rd or 4th decade of life<sup>6</sup>..."* seems to focus on "late" dysplasia. Nevertheless, that's rather a degenerative joint disease that makes the problem, not hip dysplasia itself at the third and fourth decade of life. Authors should define the term "early detection ... of late dysplasia". Do they mean the diagnosis? If so - why an "early" diagnosis is important in such "antiquated" dysplasia?

Proposed classification should be discussed in a group of investigators and practitioners, including geneticists, neonatologists, pediatricians, orthopedists, etc. Proposed treatment, albeit scanty, as well. In classification generally accepted definitions and terms should be abided by.

Paper requires linguistic improvements and English language edit.

#### **Is the topic of the review discussed comprehensively in the context of the current literature?**

Partly

#### **Are all factual statements correct and adequately supported by citations?**

Partly

#### **Is the review written in accessible language?**

Yes

**Are the conclusions drawn appropriate in the context of the current research literature?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Orthopaedic surgery, musculoskeletal trauma, bone physiology, fracture healing, malunion and non-union, skeletal infections, skeletal pathology and bone immunology

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.**

Author Response 27 Nov 2020

**Monika Piwowar**, Jagiellonian University,, Kraków, Poland

We would like to thank the reviewer for his time and the opportunity to develop the topic and explain the issues that turned out to be ambiguous and unclear on the reception of our study. The posted comments made us aware which threads in our paper should be deeply clarified. We will publish an updated version of the manuscript soon.

In our manuscript, we tried to organize many years of knowledge, documented in professional literature, which in some areas is misleading due to juggling by the terminology in some medical issues. For this reason, in the title of the manuscript, we have included the names of the main pathomechanisms of hip defects, i.e. dysplasia, deformity, malformation, which are often used as synonyms but are not. Based on the publication references, we have demonstrated the line of our reasoning and the proposed division of hip developmental defects derived from it.

It is difficult for us to argue with the reviewer because the reviewer's comments are incorrect in the assumptions themselves, which we will try to justify below. Moreover, the conceptual set we use is not consistently used in two-sided argumentation. We understand, however, where it comes from, namely from the great mess in the nomenclature in which we also found ourselves at some point, and which prompted us to organize these issues. A discussion of DDH is only possible if the debaters are based on a consensus understanding of the same concepts. Therefore, in the manuscript, we have included a number of definitions (from professional literature) so that every attentive reader has no doubts about what we are writing about and what we are referring to, and in order to precisely and unambiguously describe the issue.

We would like to emphasize the differences between dysplasia and deformation (Latin *deformatio*) in the medical sense, which perhaps in the original text of the manuscript is not emphasized enough to be properly perceived by the reviewer. In order to explain our view more clearly, we must return to the explanation of the terms we use. The interchangeable use of similar meaning words such as distortion and deformity, distortion and malformation, deformation (or deformity) and dysplasia is used in everyday language. On the level of medical considerations, however, it is not acceptable. And this is not just our opinion. Leading publication in the field of orthopedics J. P. Dormans "*Pediatric Orthopedics: Core Knowledge in Orthopedics*" in Chapter I by Steven L. Frick entitled "*Concepts of proper human growth and development in pediatric orthopedics*" explains the differences in the

concepts of dysplasia, deformation and distortion, on which we have based our considerations.

The term **dysplasia** refers to tissue whose structure is defective or poorly constructed; disturbed development causes disturbed anatomy. It is one of the four defect pathomechanisms. Following [Tachdjian's Pediatric Orthopedics [Chapter 01]], dysplasia is similarly defined, ie:

*„Dysplasias are structural defects caused by abnormal tissue differentiation as cells organize into tissues“.*

The term **deformity** (or deformation) refers to a properly developed anatomical structure that has been deformed by mechanical factors. This is another of the four defect pathomechanisms.

In the publication [Tachdjian's Pediatric Orthopedics [Chapter 01]] one can find another confirmation of the above definition:

*„Deformations are defects in the form, shape, or site of body parts caused by mechanical stress. The mechanical stress, which may be intrinsic or extrinsic, alters or distorts tissue. Because the fetus grows considerably faster than the infant, fetuses are more vulnerable to deformations“.*

**Distortion** is a pathological condition in which the shape of a part of the body has remodeled beyond the normal range. Distortion is therefore an overarching term that describes both deformation and malformation, as well as dysplasia.

In connection with the above, deformation (deformity) in medical terms can by no means be dysplasia, let alone malformation (Latin *malformatio*), but all of the above can lead to distortions of parts of the human body. The distinguishing of these terms is crucial for the correct diagnosis and subsequent therapeutic management, which is fraught with consequences. The effects of conservative or surgical treatment will be different in the case of Developmental Deformity of the Hip Joint and in the case of Developmental Dysplasia of the hip joint.

The reviewer used the term deformity to refer to malformation as synonyms. In our study, we pay attention to the fact that such processes are commonly erroneously interchangeably used. Suffice it to mention that by the term malformation some scientists describe various issues, e.g.

-> malformation as a pathomechanism of developmental defects, which is acting in the embryonic period

-> malformation as a synonym of distortion and often for this reason incorrectly called deformity (deformation), which is another pathomechanism of developmental defects completely different from malformation

-> malformation as a developmental defect

causing confusion in the interpretation of medical scientific reports. In our publication, we understand malformation as one of the four pathomechanisms of defects alongside dysplasia, deformity and disruption as defined contained in [Tachdjian's Pediatric Orthopedics [Chapter 01]]:

*„Malformation are structural defects that result from interruption of normal organogenesis during the second month of gestation“.*

**“ It is important to differentiate deformations from malformations. (...) Malformations cannot be corrected directly, whereas deformations can often be revised relatively easily either by elimination of the deforming force or by counteracting the force with stretching, casting, or bracing”.**

This particular pathomechanism only works in the embryonic period and underlies the

teratogenic hip dislocation.

The aim of the publication was to draw attention to the extent to which DDH is based on the pathomechanism of dysplasia, and to what extent on the pathomechanism of deformation, and to draw attention to the need to refine diagnostic schemes to distinguish these disease entities, which is currently not fully implemented despite the technical possibilities.

Currently, as we claim, not every officially diagnosed developmental dysplasia is in fact a disease whose pathomechanism is pure dysplasia. Some of them are most likely a developmental deformity. The evidence showing the presence of diagnostically mute and clinically mute cases supports the above thesis. For this reason, we have proposed an orderly division of DDH along with the nomenclature. We are not claiming that the division presented in our manuscript is perfect. It certainly needs discussion and perhaps modification, but we hope it will contribute to serious consideration on this topic as it seems necessary.

We hope that the description of the topics raised by the reviewer will help readers understand the essence of the matter and the need to organize the issue of DDH, as well as start discussing the extension of diagnostic schemes.

**Competing Interests:** There are no competing interests

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